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Targeted versus universal screening and decolonization to reduce healthcare-associated meticillin-resistant *Staphylococcus aureus* infection

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SUMMARY

Background: The benefits of universal meticillin-resistant *Staphylococcus aureus* (MRSA) admission screening, compared with screening targeted patient groups and the additional impact of discharge screening, are uncertain.

Aims: To quantify the impact of MRSA screening plus decolonization treatment on MRSA infection rates. To compare universal with targeted screening policies, and to evaluate the additional impact of screening and decolonization on discharge.

Methods: A stochastic, individual-based model of MRSA transmission was developed that included patient movements between general medical and intensive care unit (ICU) wards, and between the hospital and community, informed by 18 months of individual patient data from a 900-bed tertiary care hospital. We simulated the impact of universal and targeted [for ICU, acute care of the elderly (ACE) or readmitted patients] MRSA screening and decolonization policies, both on admission and discharge.

Findings: Universal admission screening plus decolonization resulted in 77% (95% confidence interval: 76–78) reduction in MRSA infections over 10 years. Screening only ACE specialty or ICU patients yielded 62% (61–63) and 66% (65–67) reductions, respectively. Targeted policies reduced the number of screens by up to 95% and courses of decolonization by 96%. In addition to screening on admission, screening on discharge had little impact, with a maximum 7% additional reduction in infection.

Conclusions: Compared with universal screening, targeted screening substantially reduced the amount of screening and decolonization required to achieve only 12% lower reduction in infection. Targeted screening and decolonization could lower the risk of resistance emerging as well as offer a more efficient use of resources.

Introduction

Healthcare-associated meticillin-resistant *Staphylococcus aureus* (HA-MRSA) infections remain a major cause of morbidity and mortality in hospitalized patients despite recent declines in several European countries.[1,2] In a large number of hospitals,

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including all 153 Veterans Affairs hospitals in the USA and all hospitals in the England and Wales National Health Service, the current practice is to screen all patients for MRSA carriage on hospital admission (a policy sometimes referred to as 'universal screening').[1,3–5] Such screening is usually accompanied by patient isolation or 'decolonization' which is the use of topical antimicrobial agents (such as mupirocin or chlorhexidine) to suppress MRSA levels and reduce the risk of progression from carriage to infection, and possibly of transmission to other patients. When used, these measures are usually applied in addition to non-specific interventions, such as enhanced hand hygiene and infection prevention and control.[3] In response to the documented long-term carriage of MRSA and its impact on hospital transmission, patients who are thought to be at risk of carrying MRSA in a number of European countries (Denmark, Norway and The Netherlands) complete a course of decolonization treatment in the community.[6–8]

Universal screening, and subsequent isolation and/or decolonization of HA-MRSA-positive patients, has the potential to be cost-effective within the intensive care unit (ICU) setting – provided resistance to decolonization treatments remains rare and interventions are effective. However, the relevance of different screening policies to lower-risk settings outside of the ICU, such as general medical wards, is less clear.[9]

HA-MRSA colonization has been shown to be associated with particular risk factors, for example, certain patient groups and medical histories; and with patient movement characteristics, such as longer than average length of hospital stay, recent hospitalization and readmission.[10,11] We hypothesized that targeting groups of inpatients with an increased length of stay or previous history of hospital admission could provide a more efficient method (in terms of screens per positive patient identified) of preventing and controlling HA-MRSA transmission, when compared with universal screening. While we recognize that the transmission of MRSA can occur in the community, we focus our research here on the transmission and control of HA-MRSA, which we refer to as MRSA for brevity.

To test this hypothesis and evaluate the impact of different screening policies on MRSA infection rates throughout the whole hospital, we performed a model-based analysis. Previous modelling work in this area has either focused on specific hospital units or used simplified representations of complex and heterogeneous patient movement patterns.[7,9,12,13] We aimed to evaluate the long-term impact of interventions in both high- and lower-risk hospital wards and to account for the impact of medical specialties and realistic patient movement patterns between different ward types and between the hospital and the community.

To characterize the complexity of patient movements within the hospital, and between the hospital and community, we analysed individual patient data and constructed a stochastic individual-based model accordingly. Using this model, we simulated MRSA transmission at an individual patient level and control in the hospital and community, and assessed the impact of targeted and universal admission and discharge screening and subsequent decolonization therapy.

Methods

Model description

We developed a dynamic, stochastic, individual-based model which simulated MRSA transmission in a hospital. Extending a previous model of a single ICU, we added non-ICU wards, populated with general medical and ACE patients, and simulated patient movements between these wards as well as a realistic patient readmission process (Figure 1A).[9] The non-ICU wards were parameterized to simulate a general medical ward. However, to avoid confusion with the general medical specialty they are referred to as non-ICU wards when discussed in the text.

The MRSA transmission and recovery processes, modelled using a previously described approach, are shown schematically in Figure 1B.[9] Parameters, adjusted for ward size, are presented in Table I. Further details of the model structure, implementation and MRSA transmission parameters process are in Appendix A.

Dataset analysis and patient movement parameters

To parameterize and inform the model we analysed an anonymized dataset of all medical patients admitted to non-ICU wards and all patients admitted to ICU wards in the Royal Free Hospital, London between 29 October 2009 and 18 May 2011. Patient movement characteristics: length of stay, daily probability of discharge, probability of ward transfer and probability of readmission, were calculated for each ward type and for both ACE and general medical specialties. Mean values are presented in Table I. Daily probabilities of discharge were adjusted to account for the increased length of stay associated with MRSA infection using previously described methods.[14] Further details of the data analysis are in Appendix B and model parameterization in Appendix C.

Identification of risk groups and formulation of intervention policies

The groups of patients targeted for intervention were identified in two stages. The first-stage analysis of the anonymized dataset showed that ACE patients had a longer than average length of stay and higher rate of readmission, and that all patients on their second or further admission had a higher risk of subsequent readmission. We therefore included these patient characteristics (different movement patterns for ACE patients, and admission history-based readmission probabilities) explicitly in the model design. Further details on the identification of high-risk patients through data analysis are in Appendix B. The second stage of identification, a baseline simulation of MRSA transmission and patient movement using the individual-based model, showed that three patient groups maintained a high prevalence of MRSA colonization and infection incidence simply due to their movement patterns. These were identified as high-risk groups for targeted screening and intervention: (i) readmitted patients discharged from hospital within the previous 365 days; (ii) patients in the ICU; and (iii) ACE specialty patients. In the baseline simulations, MRSA decolonization was only applied to clinical cases of MRSA infection. All screening policies are detailed in Table II; we assume 100% compliance with the policies. Patients who screened MRSA positive underwent MRSA decolonization treatment either in hospital or, if screened positive upon discharge, in the community. The decolonization parameters were derived from a previous

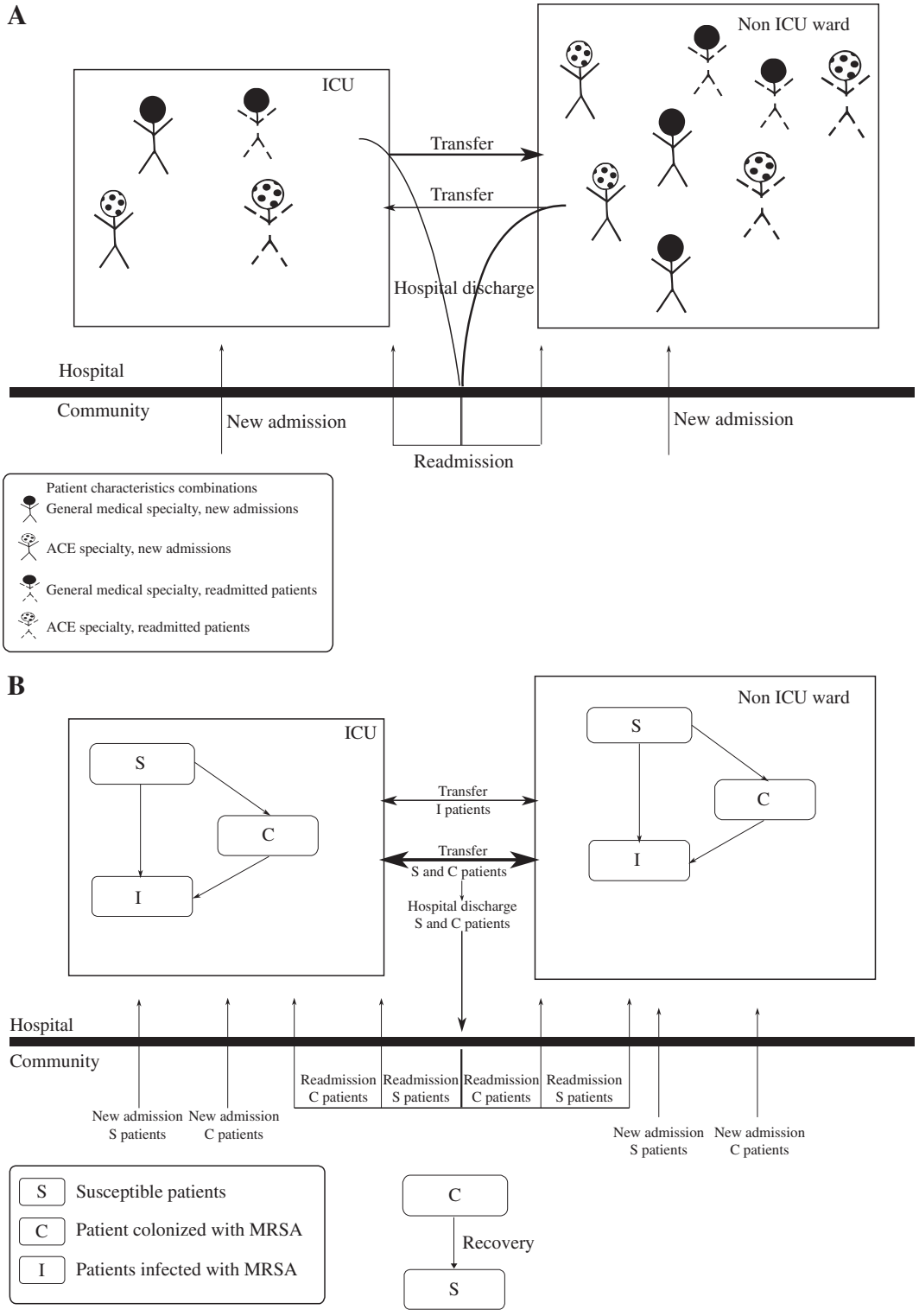

Figure 1. Schematic diagram of (A) patient movement dynamics and (B) meticillin-resistant *Staphylococcus aureus* (MRSA) transmission dynamics within the hospital and community. (A) Admission from the community (new admission and readmission), discharge and transfer from the intensive care unit (ICU) and from the rest of the hospital. Thickness of lines represents the relative frequency of the movement process. On admission, patients fill a vacated space either in the ICU or in non-ICU ward and are assigned to the general medical or acute care of the elderly (ACE) specialty (as described in Appendix A). (B) Transmission dynamics in the ICU and non-ICU wards. Transitions between these infection states are shown by solid lines. In the community only recovery from MRSA colonization can occur.

Table I
Model parameters

Parameter	ICU	Non-ICU wards		All wards	Source
	All specialties	ACE specialty	General medical specialty	All specialties	
Ward and hospital discharge					
Daily probability of ward discharge for susceptible and MRSA-colonized patients	0.13	0.13	0.15		Mean of a distribution used in model, estimated from individual-level hospital data. Full distribution presented in Appendix C.
Daily probability of ward discharge for MRSA-infected patients	0.08	0.09	0.12		Mean of a distribution used in model, estimated from individual-level hospital data. Full distribution presented in Appendix C.
Daily probability of hospital discharge given a ward discharge	0.18	0.58	0.51		Mean of a distribution used in model, estimated from individual-level hospital data. Full distribution presented in Appendix C.
Daily probability of transfer between ward types	0.56	0.0036	0.00053		Mean of a distribution used in model, estimated from individual-level hospital data. Full distribution presented in Appendix C.
Daily probability of death for susceptible and MRSA-colonized patients	0.02	0.007			ICU ward: mean of a 21-day distribution used in model; full distribution and method of estimation presented by Robotham et al.[9]; non-ICU ward: per-day probability estimated as described in Appendix A
Daily probability of death for MRSA-infected patients	0.03	0.0085			ICU ward: mean of a 21-day distribution used in model; full distribution and method of estimation presented by Robotham et al.[9]; non-ICU ward: per-day probability estimated as described in Appendix A.
Readmission					
Probability of readmission					
1st hospital stay	0.26	0.31	0.26		Estimated from individual-level hospital data as described in Appendix B.
2nd hospital stay	0.50	0.67	0.50		Estimated from individual-level hospital data as described in Appendix B.
Time (days) between discharge and readmission (mean)				96.69	Mean of a distribution used in model, estimated from individual-level hospital data. Full distribution presented in Appendix C.
Probability that a patient will be readmitted to the same specialty	1	0.18	1		Estimated from individual-level hospital data.
Hospital population					
Prevalence of MRSA on first admission				0.03	Literature[11]
Proportion of patients assigned to ACE specialty				0.30	Estimated from individual-level hospital data
Hospital beds	20	880			Hospital data
Transmission					
Daily probability of cross-colonization per source	0.00185	0.000049			ICU[9]; non-ICU wards: estimated as described in Appendix A.
Daily probability of cross-infection per source	0.0003	0			ICU[9]; non-ICU wards: estimated as described in Appendix A.

Table I (*continued*)

Parameter	ICU	Non-ICU wards		All wards	Source
	All specialties	ACE specialty	General medical specialty	All specialties	
Daily probability of progression from colonization to infection	0.047	0.016			ICU[9]; non-ICU wards: estimated as described in Appendix A.
Duration of colonization (mean)				365 days	Exponentially distributed with a mean of 365 days.[6,17]
Duration of infection				Until discharge	Assumption
Screening					
Sensitivity					
Baseline intervention (clinical cultures)				0.68	Values assume the use of conventional culture[9]
Policies 2–25 (screening)				0.83	Values assume the use of chromogenic agar[9]
Specificity					
Baseline intervention (clinical cultures)				0.88	Values assume the use of conventional culture[9]
Policies 2–25 (screening)				0.83	Values assume the use of chromogenic agar[9]
Turnaround time (days)					
Baseline intervention (clinical cultures)				4	Values assume the use of conventional culture[9]
Policies 2–25 (screening)				3	Values assume the use of chromogenic agar[9]
Decolonization (mupirocin and chlorhexidine treatment for 5 days)					
Proportion of treated patients who are MRSA negative at treatment end				0.69	Estimated as described in Appendix D.
Daily probability of reversion to MRSA-positive status for successfully treated patients				0.13	Estimated as described in Appendix D.
Proportional reduction in susceptibility to colonization given exposure to one colonized or infected patient				0.65	[9]
Proportional reduction in susceptibility to infection given exposure to one colonized or infected patient				0.66	[9]
Proportional reduction in daily probability of progression or self-infection				0.31	[9]

ICU, intensive care unit; MRSA, meticillin-susceptible *Staphylococcus aureus*; ACE, acute care of the elderly.

study, assuming use of both chlorhexidine and mupirocin in the absence of resistance to these agents; further details are provided in Appendix D.[9] The probability of relapse to an MRSA-colonized state for a patient decolonized at the end of treatment was estimated using a simple deterministic model, parameterized from a literature search; this is described in Appendix D. Policy assessments were based on 500 simulation runs, for 10 years, discarding the first year's results to allow MRSA and patient dynamics to reach equilibrium. The mean of the remaining nine-year reporting period was taken for all outcome statistics. The reported 95% coverage intervals (CIs) for outcome statistics represent the 2.5th and 97.5th percentiles from the resulting distributions.

Results

Output from baseline simulation of individual-based models

In baseline model simulations, the mean rate of MRSA infection was 52.4 (95% CI: 51.5–53.2) per 10,000 bed-days in

Table II
Policy number and target groups

Policy no.	Screening and decolonization of:
Single	
1	Baseline: No screening: treatment of clinical cases only
2	All patients on admission and weekly until discharge
3	All patients on admission
4	Patients discharged from hospital 365 days previously on admission and weekly until discharge
5	Patients discharged from hospital 365 days previously on admission
6	Patients in ACE specialty on admission and weekly until discharge
7	Patients in ACE specialty on admission
8	ICU patients on admission and weekly until discharge
9	ICU patients on admission
10	All patients on discharge
11	Patients discharged from hospital 365 days previously on discharge
12	Patients in ACE specialty on discharge
13	ICU patients on discharge
Combined	
14	Policies 4 and 10
15	Policies 4 and 11
16	Policies 4 and 12
17	Policies 4 and 13
18	Policies 6 and 10
19	Policies 6 and 11
20	Policies 6 and 12
21	Policies 6 and 13
22	Policies 8 and 10
23	Policies 8 and 11
24	Policies 8 and 12
25	Policies 8 and 13

ACE, acute care of the elderly; ICU, intensive care unit.

the ICU and 1.6 (1.6–1.7) per 10,000 bed-days in the whole hospital including ICU wards. On average 8.1% (8.1–8.1) of all patients, 9.7% (9.7–9.7) of ACE specialty patients and 14.2% (14.2–14.3) of readmitted patients discharged from hospital within the previous 365 days were colonized on admission. Of all patients, 14.8% (14.8–14.9) were discharged while MRSA-colonized. Of these patients, ACE and those with a prior admission within 365 days of the current one had respective probabilities of 46.4% (46.3–46.4) and 48.7% (48.5–48.8) of returning to the hospital while still colonized. Combined, these patients constituted the majority (93%) of patients who remained colonized on a subsequent hospital admission (Table III).

Impact of targeting risk groups

Screening all patients on admission and weekly thereafter until discharge (policy 2) resulted in the largest [77% (95% CI: 76–78)] net reduction in MRSA infection in the whole hospital over a nine-year period and a 76% (75–77) reduction in the ICU (Figure 2A). However, the policy required screening 207.6 (207.4–207.7) patients per day and prevented one MRSA infection for every 9700 screens (Figure 2C). By contrast, policy 8 (screening patients admitted to the ICU and weekly thereafter until discharge) resulted in screening 8.6 (8.5–8.7) patients per day, for a 73% (72–74) reduction in MRSA infections in the ICU and 66% (65–67) reduction in the whole hospital (Figure 2A). This policy prevented one MRSA infection in the ICU for every 89 screens, and one infection in the whole hospital for every 103 screens. This resulted in a reduction in the number of screens carried out by 95% and courses of decolonization treatment by 96% when compared with policy 2.

However, policy 8 reduced the number of total colonized bed-days over nine years by only 25.4% (95% CI: 25.0–25.8), whereas policies targeting the other risk groups: readmitted patients discharged from hospital 365 days previously, and ACE specialty patients (policies 4 and 6, respectively); achieved 43% (43–43) and 56% (55–56) reductions in colonized bed-days and 57% (55–59) and 62% (61–63) net reductions in MRSA infection, respectively. Policies 4 and 6 screened 59 (59–59) and 79 (79–79) patients per day respectively, therefore reducing the number of screens by 72% (policy 4) and 66% (policy 6), and reducing the number of decolonization treatments by 55% (policy 4) and 45% (policy 6) compared with policy 2.

Impact of community decolonization

Screening and decolonization of patients upon discharge decreased the proportion of patients colonized on admission by between 76% (policy 13) and 76% (policy 10). However, further reductions in MRSA infection rates were <1% for policies 14–16, 18–20 and 22–25 (Figure 2B) when additional screening on discharge was implemented compared with screening on admission alone. An exception to this was policy 17, which targeted readmitted patients who had been discharged from hospital 365 days previously on admission and additionally screened ICU patients on discharge, which achieved an

Table III
Proportion of colonized patients from each risk group; results from baseline simulation

Risk group	Colonized on admission	Colonized on discharge	Readmitted colonized[a]
Readmitted[b]	0.67 (0.64–0.67)	0.44 (0.43–0.44)	0.49 (0.49–0.49)
ACE specialty[c]	0.31 (0.30–0.31)	0.49 (0.49–0.49)	0.46 (0.46–0.46)
ICU ward[d]	0.02 (0.02–0.03)	<0.01	<0.01

ACE, acute care of the elderly; ICU, intensive care unit. Values are mean (CI).
[a] Proportion of patients discharged colonized who will be readmitted colonized from each risk group.
[b] Readmitted patients discharged from hospital less than 365 days previously to the current admission.
[c] Patients assigned to the ACE specialty.
[d] Patients admitted to an ICU (colonized on admission) or discharged into the community from the ICU ward (colonized on discharge).

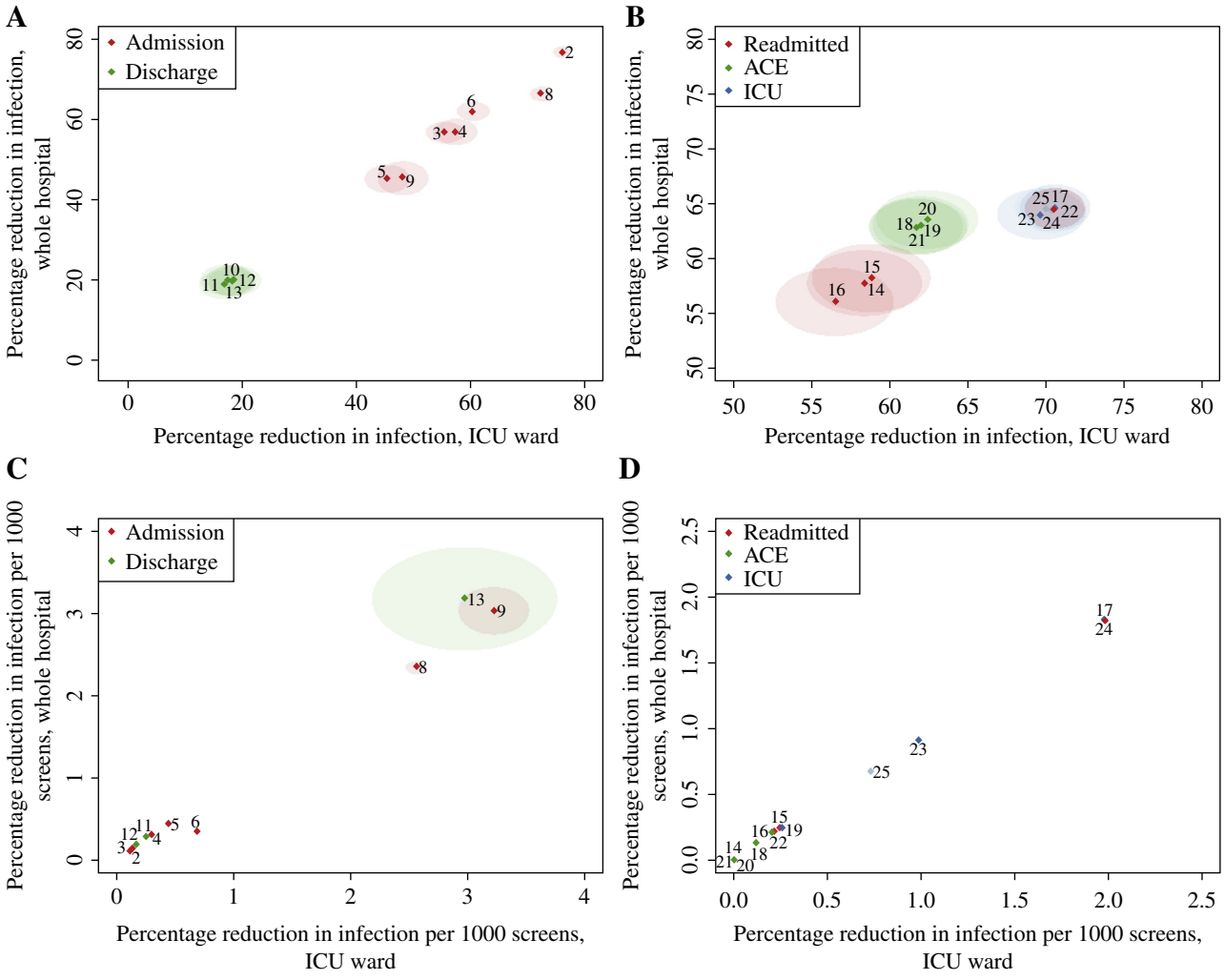

Figure 2. (A, B) Percentage reduction in infection in the intensive care unit (ICU) and in the whole hospital for each policy compared with the baseline. (C, D) Percentage reduction in infections per 1000 screens in the ICU ward and whole hospital compared with the baseline. (A, C) Single Policies (2–13) in which targeted screening and decolonization occur only on admission (red points) or discharge (green points). (B, D) Combined Policies (14–25) in which targeted screening and decolonization occur on admission and additionally on discharge. Policy numbers correspond to the policy descriptions listed in Table II. Solid points plot the mean percentage reduction in infections. Transparent ellipses plot the 95% coverage intervals from 100 model simulations. Colours represent populations targeted for screening and decolonization.

additional 7% (95% CI: 3–7) reduction in infection (Figure 2B) compared with screening patients on admission alone.

Discussion

Previous models of MRSA transmission have examined a multi-ward setting within a hospital with limited patient movement dynamics.[13,15] The model presented here is, to our knowledge, the first attempt to account for the effect of heterogeneous patient movement patterns associated with different specialties and ward types on MRSA transmission dynamics and the effect of screening and decolonization. The detailed description of patient movements both within the hospital and between the hospital and community should allow a more realistic representation of the overall transmission dynamics. For example, high-risk groups in the non-ICU wards maintained a high prevalence of MRSA colonization (ACE medical specialty 25% and readmitted patients 21%) purely through their increased length of stay and high probability of readmission. The inclusion of the 'feedback loop' between hospital and community populations, created by readmitted patients, also allowed the evaluation of the long-term effects of interventions, as well as the impact of community control on the hospital dynamics. The results of the baseline simulation were consistent with rates of MRSA infection reported through mandatory surveillance before the decline in MRSA infection rates from 2005 onwards, as was the relative prevalence of MRSA colonization on admission in readmitted and ACE specialty patients.[16]

We selected risk groups based on high rate of MRSA infection (ICU wards) and the increased prevalence of MRSA colonization (ACE specialty and readmitted patients). Due to their high prevalence of colonization and higher probability of readmission, ACE medical specialty and readmitted patients made up the majority of patients who returned to hospital while still

colonized with MRSA. Targeting these patient groups reduces hospital transmission which, in turn, results in fewer patients with MRSA on admission.

Whereas universal screening and decolonization likely played a role in the reduced hospital rates of MRSA infection, it resulted in a substantial screening and treatment burden. In addition to the allocation of financial and human resources that universal screening requires, subsequent mass decolonization may place a selection pressure for the development of resistance to commonly used agents such as mupirocin or chlorhexidine. We show that targeting specific hospital patients with a high risk of infection (such as those in ICU) substantially reduces the screening burden and number of decolonization treatments while resulting in only a 12% smaller reduction in infection compared with universal screening. In low-risk settings (i.e. non-ICU wards), targeting ACE patients reduced the burden of screening and treatment by half, yet resulted in only an 8% smaller reduction in infection compared with universal screening. Therefore inappropriate use of decolonization will be decreased with a targeted screening system as fewer false positives will be treated with mupirocin/chlorhexidine. Hence targeted screening could lower the risk of resistance emerging as well as offering a more efficient use of resources. Given that MRSA carriage may persist for well over a year in a single patient, screening and successful decolonization on discharge may help to reduce the burden of MRSA colonization in readmitted patients.[6] We found, however, that the additional benefit of decolonization on discharge on the rate of MRSA infection in the hospital was limited compared with intervention during the hospital stay.

One limitation of our model was that we did not consider MRSA transmission and infection in surgical wards. Although surgery is a high-risk setting for infection, this exclusion is necessitated by the lack of data to estimate parameters needed to simulate patient movement and MRSA transmission robustly within such wards. Another limitation was that we did not account for variation in the persistence of MRSA carriage in different patient groups or heterogeneity of infection sites. We have considered MRSA infection as a single type of event, but MRSA infection can occur in multiple sites and the impact of different policies may depend of the distribution of infection types. The model did not consider the risk of universal decolonization adding to the development of resistance to decolonization agents. Although the prevalence of resistance to mupirocin and chlorhexidine remains low, some studies document treatment failure associated with resistance.[18–20] However, restricting the use of mupirocin and/or chlorhexidine to a smaller number of patients through targeted screening and treatment, as we suggest here, is likely to reduce selection for resistance. Further, if the benefit of screening and treatment of all patients declines over time (e.g. due to reduced MRSA prevalence), our findings that support targeted rather than universal screening are strengthened.

Conflict of interest statement
None.

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Appendix A

Model structure and implementation

The model was stochastic, discrete time (with a time unit of one day) and individual-based. It tracked the MRSA status and hospital exposure of a group of 100,000 individuals, 920 of whom were assumed to be hospitalized at any one time. Each individual had a number of associated attributes which were updated every day. These attributes were: current MRSA status [colonized, infected or MRSA free (susceptible)]; date therapy to suppress MRSA carriage started (if currently in use); current hospitalization status; time since the most recent hospital admission; time since most recent hospital discharge; ward type (ICU or non-ICU if currently hospitalized); medical specialty and whether the patient had been discharged from hospital less than 365 days previously. These characteristics determined a patient's hospital movement parameters, the probability of discharge and readmission on each day of stay and identified patients as targets for intervention strategies.

Medical specialty and a tag corresponding to whether a patient had been discharged from hospital 365 days previously (readmission status) were assigned on hospital admission, and retained for the rest of the hospital stay. Seventy percent of patients were assigned to the general medicine specialty on their first admission. The remainder were assigned to the acute care of the elderly (ACE) medical specialty. The specialty of patients was retained on a subsequent hospital admission with a specified probability (Table I). Patient movement parameters were calculated directly from a de-identified dataset of all patients admitted to the 900-bed Royal Free National Health Service Trust Hospital, London, between 29 October 2009 and 18 May 2011. These parameters are presented in Table I.

Readmitted patients were assigned to one of two groups: patients who had been discharged from the hospital within 365 days prior to the current hospital admission; and 'new admissions' or those patients who had last been discharged from hospital more than a year previously.

Once discharged to the community, patients could be readmitted to hospital at some time in the future. The readmission process was parameterized to reflect the patient movement patterns seen in real hospital data, where the probability of readmission increased after a second hospital visit. The probability that a patient was readmitted was dependent on the hospital visit number and the medical specialty; these parameters are presented in Table I. If scheduled for readmission, a patient's MRSA status on discharge was retained. Clearance could occur during the time between hospital discharge and readmission (Table I).

The model was implemented in C++. The model was run for 10 years in each simulation; the first year's results were disregarded to allow MRSA and patient dynamics to reach equilibrium. Five hundred simulation runs were performed for each policy. Ninety-five percent coverage intervals (CIs) were calculated for outcome statistics and represent the 2.5th and 97.5th percentiles from the resulting distributions.

MRSA transmission dynamics

The MRSA transmission and recovery processes were derived from previously described single ward processes.[1] Each day,

patients could transition between three possible states: susceptible; MRSA-colonized; and MRSA-infected. It was assumed that the probability of a susceptible patient becoming colonized (in non-ICU and ICU wards) or infected directly from susceptible status (in ICU wards only through cross-infection) increased linearly with the number of MRSA-positive patients (both colonized and infected) on their ward. As described in Table A-I, each day the probability that patient *m* in ward *i* transitions from susceptible to MRSA-colonized/infected depends on the total number of colonized or infected patients in that ward on that day and the daily individual probability of cross-colonization (θ) or infection (ι) per source in ward *i*, i.e. daily patient susceptibility to colonization and infection. Each day a patient *m* in ward *i* will transition from susceptible to colonized if

$$ran < 1 - (1 - \theta_i)^{\sum(C_i(t)+I_i(t))},$$

from susceptible to infected if

$$ran < 1 - (1 - \iota_i)^{\sum(C_i(t)+I_i(t))},$$

and from colonized to infected if $ran < \rho_i$, where *ran* is a number randomly and repeatedly drawn from a uniform distribution (see Table A-I for parameter definitions). We assumed that all colonized and infected patients were equally infectious and that transmission occurred via a mass action process. MRSA-colonized patients could also progress to MRSA infection through self-infection, i.e. progression from a colonized to an infected state, at a daily probability ρ_i. Although colonized and infected patients could transfer between wards, the transmission dynamics of each ward were otherwise independent.

Recovery from MRSA colonization and infection

At the time of colonization or infection, the recovery date for the patient was selected from an exponential distribution with a mean of 365 days. A patient could be discharged colonized from the hospital but an infected patient was assumed to revert to a colonized state on discharge. The use of decolonization overrode the natural recovery processes.

MRSA transmission parameters

Transmission parameters specific to the ICU wards used in the simulations were taken from previously published research.[1] Transmission parameters specific to the non-ICU wards were the same as those previously used to describe general medical wards by Robotham *et al.*, where estimates of the daily probability of colonization and infection given exposure to one MRSA-positive patient were derived from previous work fitting a continuous time multistate Markov model to MRSA surveillance and infection data.[1,2]

Estimation of daily probability of death

The daily probability of death for patients (with and without MRSA infection) in ICU had been estimated in previous research using a time-dependent model.[3] Estimates for the non-ICU ward were taken from previous research.[2] The method of estimation is described in brief here. Using Dr Foster data 2008/2009 (for East of England trusts, from Eastern Region Public Health Observatory), the standardized mortality rate per 1000 discharges in general medicine was 44.7. Assuming a mean length of stay in general medicine of 6.3 days (Hospital Episode Statistics 2008/2009), this would give a daily death probability of 0.007. The death rate was adjusted to account for MRSA infection using the method described by Robotham *et al.*[1]

Table A-I
Daily transmission transition probabilities and mechanism of decolonization

Transition	Transition probability of patient *m* on day *t*	Decolonization impact
$S_i \rightarrow C_i$	$1 - (1 - \theta_i)^{\sum(C_i(t)+I_i(t))}$	$\theta_i = \theta_i(1 - \delta_c)$
$S_i \rightarrow I_i$	$1 - (1 - \iota_i)^{\sum(C_i(t)+I_i(t))}$	$\iota_i = \iota_i(1 - \delta_i)$
$C_i \rightarrow I_i$	ρ_i	$\rho_i = \rho_i(1 - \delta_p)$

S_i, susceptible patient in ward *i*.
C_i, colonized patient in ward *i*.
I_i, infected patient in ward *i*.
θ_i, daily probability of cross-colonization per source in ward *i*.
ι_i, daily probability of cross-infection per source in ward *i*.
ρ_i, daily probability patient will progress from colonization to infection.
δ_c, reduction in susceptibility to colonization given exposure to one colonized or infected patient.
δ_i, reduction in susceptibility to infection given exposure to one colonized or infected patient.
δ_p, reduction in probability of progression to infection given patient is colonized.

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Appendix B. Data analysis results

The length of stay in a ward ranged from less than one day to 174 days, with the majority of patients discharged from a ward by the end of day 2 (63%, 8319/13105). The median length of ward stay was 1 day [interquartile range (IQR): 0–4] for patients in non-ICU wards and 6 days (IQR: 2–13) for patients in ICU wards. The median length of stay in the hospital as a whole was 5 days (IQR: 2–11). This increased to 12 days (IQR: 4–12) for patients with at least one ICU episode during their hospital stay.

We explored the dataset to examine heterogeneity in length of stay among the main specialties. Of the two most common specialties in the dataset (general medicine and ACE), patients admitted to the ACE specialty had a median length of ward stay of 3 days (IQR: 1–7) and a hospital stay of 9 days (IQR: 4–17). Patients admitted to the general medicine specialty had an average length of ward stay of 1 day (IQR: 0–3) and hospital stay of 3 days (IQR: 2–7).

We estimated the probability of readmission to hospital within 365 days of discharge. We excluded all hospital admissions on or after 20/05/2010, i.e. 365 days before the last admission recorded in the dataset. This restricted the dataset to 975 hospital admissions. For this group, 31% of patients were readmitted within 365 days of discharge. The probability of readmission increased with each additional hospital stay; 22% of patients newly admitted to hospital went on to be readmitted within 365 days of discharge, whereas 58% of patients attending for their second or subsequent hospital stay within a one-year period were readmitted.

The distribution of time between hospital stays was right-skewed. Of those patients who were readmitted within 365 days of discharge, the median length of time between discharge and readmission was 58 days (IQR: 17–149).

We restricted analysis of heterogeneity in readmission rates to the two most common specialties: general medicine and ACE. The probability of readmission within one year of discharge for general medicine patients was 0.20 (95% CI: 0.18–0.21), compared with 0.31 (95% CI: 0.26–0.35) for those assigned an ACE specialty. The length of time between discharge and readmission had a median of 27 days (IQR: 12–99) for the ACE specialty and 17 days (IQR: 7–34) for the general medicine specialty. Using the χ^2-test we found no significant difference ($P > 0.9$) between these two specialties in the distribution of time between discharge and the next hospital admission.

Based on the above analysis the following patient groups were identified as at risk of MRSA colonization/infection due to their movement patterns: patients admitted to the ICU (due to increased length of ward and hospital stay); patients admitted to the ACE specialty (due to increased length of ward and hospital stay and increased probability of prompt readmission following discharge); and patients with a previous hospital admission within the previous 365 days (due to increased probability of further readmissions).

Table C-II
Daily probability of transfer from or to an ICU ward, conditional on discharge from a ward but not the hospital

Day	Non-ICU ward to ICU	ICU to non-ICU ward
1	0.004	0.625
2	0.002	0.818
3	0.001	0.778
4	0.001	0.750
5	0.002	0.643
6	0.001	0.625
7	0.002	0.625
8	0.002	0.625
9	0.002	0.625
≥10	0.001	0.625

Table C-III
Daily probability of hospital discharge when a patient is discharged from a ward, conditional on discharge from the ward that day

Day	ICU ward	Non-ICU ward	
	General medicine and ACE specialties	ACE specialty	General medical specialty
1	0.063	0.727	0.666
2	0.156	0.404	0.538
3	0.188	0.410	0.544
4	0.203	0.482	0.552
5	0.205	0.510	0.529
6	0.186	0.528	0.534
7	0.207	0.670	0.528
8	0.181	0.565	0.571
9	0.173	0.660	0.402
10	0.178	0.617	0.429
11	0.192	0.727	0.462
12	0.200	0.404	0.365
13	0.185	0.410	0.265
≥14	0.171	0.482	0.313

Appendix C. Discharge distributions

Table C-I
Daily probability of discharge from a ward by the end of each day for patients in ICU and an non-ICU ward

Day	ICU ward: all specialties (general medicine and ACE)		Non-ICU ward: ACE specialty		Non-ICU ward: general medicine specialty	
	Susceptible and MRSA-colonized patients	MRSA-infected patients	Susceptible and MRSA-colonized patients	MRSA-infected patients	Susceptible and MRSA-colonized patients	MRSA-infected patients
1	0.085	0.052	0.242	0.146	0.583	0.352
2	0.168	0.092	0.169	0.093	0.323	0.177
3	0.236	0.126	0.201	0.107	0.289	0.154
4	0.176	0.099	0.192	0.107	0.258	0.144
5	0.161	0.093	0.171	0.099	0.243	0.141
6	0.128	0.079	0.150	0.092	0.202	0.124
7	0.073	0.048	0.115	0.076	0.225	0.149
8	0.079	0.055	0.130	0.090	0.18	0.125
9	0.143	0.099	0.134	0.093	0.175	0.121
10	0.200	0.137	0.122	0.083	0.179	0.122
11	0.042	0.030	0.103	0.073	0.211	0.15
12	0.043	0.030	0.130	0.067	0.144	0.101
13	0.182	0.124	0.242	0.069	0.158	0.108
≥14	0.056	0.038	0.169	0.063	0.118	0.079

Table C-IV
Distribution of times between discharge and readmission

Month since discharge	Proportion of patients readmitted
1	0.26
2	0.19
3	0.16
4	0.14
5	0.10
6	0.04
7	0.06
8	<0.01
9	0.05
10	<0.01
11	0.01
12	<0.01

Appendix D. Topical MRSA suppression (decolonization) process and parameters

Topical MRSA suppression chemotherapy (sometimes referred to as 'decolonization', and often making use of agents such as mupirocin and chlorhexidine) may (i) reduce the daily probability of acquiring MRSA if a treated patient is susceptible at the beginning of treatment; (ii) reduce the daily probability of transmission of MRSA from a colonized/infected patient undergoing treatment; and (iii) reduce a colonized patient's probability of progression to MRSA infection while undergoing treatment (the computational process is shown in Table A-I).

Parameter estimates for all three effects were taken from a previously described study assuming a five-day course of chlorhexidine gluconate and mupirocin and full susceptibility to these agents.[1]

The probability that MRSA suppression chemotherapy cleared MRSA carriage (causing an MRSA-colonized or infected patient to revert to susceptible status and the probability that apparently successfully treated patients (who were not colonized with MRSA at the end of treatment) became recolonized with MRSA before they were readmitted to hospital were estimated from aggregate data collected as part of a literature review (following the search criteria and selection method outlined by Robotham *et al.*[1]). We developed a simple model (Equations 1 and 2) in which a group of patients undergoing treatment, recovered from MRSA colonization due to successful treatment, and successfully treated patients could become recolonized with MRSA.

Equation 1:

$$\frac{d}{dt}(C) = \delta S - \tau\sigma C$$

Equation 2:

$$\frac{d}{dt}(S) = \tau\sigma C - \delta S$$

where:
C, colonized patients;
S, susceptible patients;
$N = C + S$, population of treated patients;
δ, probability of reversion to MRSA-positive status for successfully treated patients within one year;
τ, rate of treatment completing (1/Duration of treatment) where duration of treatment is five days;
σ, proportion of treated patients who are MRSA negative at treatment end.

The model was fitted applying a least-squares method to the collated proportion of treated patients that were MRSA susceptible over time.[2–5] The proportion of successfully treated patients and the probability of reversion to an MRSA-positive status for successfully treated patients are presented in Table I (main paper). The decolonization effectiveness parameters were assumed to be the same in the ICU and non-ICU settings and in the community.

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